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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/830,706	08/07/2001	Shingo Toji	55865	1848

7590 12/03/2003  
Edwards & Angell, LLP  
101 Federal Street  
Boston, MA 02110

EXAMINER
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PAK, YONG D

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 12/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/830,706	<b>Applicant(s)</b> TOJI ET AL.	
	<b>Examiner</b> Yong D Pak	<b>Art Unit</b> 1652	

**-- Th MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE \_\_\_\_ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☐ Claim(s) \_\_\_\_ is/are pending in the application.  
     4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) \_\_\_\_ is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. §§ 119 and 120**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
     a) ☐ All    b) ☐ Some \*    c) ☐ None of:  
         1. ☐ Certified copies of the priority documents have been received.  
         2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.  
         3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
     a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). ____.  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                    | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____. | 6) <input type="checkbox"/> Other: _____                                    |

### **DETAILED ACTION**

The amendment filed on October 14, 2003, amending claims 1-3, has been entered.

Claims 1-19 are pending.

### ***Election/Restrictions***

Applicant's election with traverse of Group I (claims 1-5) with a further election of SEQ ID NO: 1 and 2 is acknowledged. The traversal is on the ground(s) that Groups I-V share a special technical feature and that the two thioredoxin reductases share a common structure and function. This is not found persuasive because in the requirement for restriction was based on claims presented as filed and applicant has already received an action on the merits for the originally presented invention.

Regarding the two thioredoxin reductases, even though the two proteins are similar in structure and function, the two proteins are patentably distinct because their structure is different. The two proteins have different physical and chemical properties and different substrate specificity.

Further, for a DNA and protein group to share a special technical feature, claims drawn to the DNA must be DNA sequences that encode the structure of the protein in the claims drawn to the protein (see PCT administrative instructions Example 17). IN the instant invention, the DNA and proteins claims to not correspond to each other in that claim 8 is drawn to DNA encoding the protein of SEQ ID NO:1 while claims 2-4 are

drawn to variants of the protein of SEQ ID NO:1. Therefore, the technical feature linking Group I-V is lacking.

The requirement is still deemed proper and is therefore made FINAL.

Claims 6-19 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement.

### ***Claim Objections***

Claims 1-5 are objected for being drawn to non-elected products, SEQ ID NOs: 3 and 4.

### ***Priority***

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

### ***Information Disclosure Statement***

The information disclosure statements (IDS) submitted on February 24, 2003, October 15, 2002, July 16, 2002 and January 8, 2002 are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-5 are rejected under 35 U.S.C. 101 because the claimed invention is directed to a non-statutory subject matter. Claims 1-5 read on a product of nature. This rejection can be overcome by amending claims 1-5 as "An isolated protein...", for example.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2 and 4 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 2 is drawn to DNA that is at least 60% identical to DNA encoding SEQ ID NO:2. A description of roughly over half of the whole structure of DNA encoding SEQ ID NO:2 amounts to insufficient description of the structure of the DNA molecule in this claim. Therefore, these claims are drawn to a large variable genus of DNA molecules encoding polypeptides having an insufficient limitation on structure. The specification does not describe the function of all the polypeptide sequences encoded by the DNA molecules derived or modified from SEQ ID NO:1 and therefore, many functionally

unrelated polypeptides are encompassed within the scope of these claims. Therefore, the specification fails to describe representative species by any identifying characteristics other than being the functionality of encoding a thioredoxin reductase having XIAP-binding activity.

Claim 4 is drawn to a thioredoxin reductase wherein the protein is modified by one or more amino acid deletion, addition, insertion, or substitution. The single species of the thioredoxin reductase of SEQ ID NO:2 is insufficient to describe the whole genus containing a vast number and combinations of amino acid deletions, insertions, additions, or substitutions. The specification fails to place limitations on the thioredoxin reductase structure or disclose which amino acid(s) of SEQ ID NO: 2 can be safely modified and still impart thioredoxin reductase activity. Therefore, the specification fails to describe other representative species from other sources or by identifying characteristics or structural properties other than the functionality of encoding a polypeptide with thioredoxin reductase activity.

Given this lack of the description of the representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the inventions of claims 2 and 4.

Claims 2 and 4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for DNA encoding the thioredoxin reductase of SEQ ID NO:2, does not reasonably provide enablement for DNA molecules encoding a

thioredoxin reductase that is not homologous to 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The claims encompass DNA molecules encoding a thioredoxin reductase having very low structural similarity to SEQ ID NO:2. The structural limitation is as follows: 60% of the whole structure of SEQ ID NO:2. Despite knowledge in the art for isolating polynucleotides, the specification fails to provide guidance regarding which amino acids of SEQ ID NO:2 are required to impart a polypeptide as a thioredoxin reductase. Therefore, these claims encompass reductases having structures with low homology to SEQ ID NO:2. Therefore, the breadth of these claims is much larger than the scope enable by the specification.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity are limited in any

protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification, which places weak limitation on the structure of the polypeptides as discussed above, does not support the broad scope of the claims because the specification does not establish: (A) regions of the thioredoxin reductase structure which may be modified without effecting reductase and XIAP activity; (B) the general tolerance of to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

In the state of the art, the function of a polypeptide is unpredictable from its structure and the functionality of a polypeptide must be known in order to use the polypeptide. Therefore, the specification does not teach how to use polypeptides with unknown function.

Therefore, one of ordinary skill would require guidance in order to make DNA encoding a thioredoxin reductase with structures different from SEQ ID NO:2 and how to use DNA encoding polypeptides having unknown function in a manner reasonable correlated with the scope of the claims. Without such guidance, the experimentation left to those skilled in the art is undue.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.



Claims 1-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The mere recitation of the name "XIAP" is insufficient to convey with clarity that which applicant sees as the invention.


No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 703-308-9363. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Yong D. Pak  
Patent Examiner

  
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